**TRANSGENIC MICE: PREPROENKEPHALIN AND μOPIATE RECEPTOR.** G. R. Uhl@#%, D. M. Donovan#, B. O'Hara!, J. Mulle#, L. Sharpe#, C. Schindler*, E. Unterwald$, L. Miner#. #Molecular Neurobiology, *Preclinical Pharmacology, %Office of the Director, Div. of Intramural Research, NIDA; $Rockefeller Univ.; !Stanford Univ.; @Depts. of Neurol. & Neurosci., JHUSM, Balto., MD 21224

Endogenous brain systems mediating analgesia and reward principally employ enkephalin recognition by mu opiate receptors. Transgenic mice reveal promoter elements mediating tissue-specific expression and regulation and consequences of altered expression of these two genes.

Transgenic mice express a chloramphenicol acetyltransferase (CAT) reporter in a tissue-specific pattern under the control of short regions of the human preproenkephalin A gene 5' flanking region. CNS transgene expression is regulated by two stimuli that regulate expression of the wild type preproenkephalin gene, sensory stimulation and neuroleptics. Animals expressing 15 kb of the rat preproenkephalin A gene, including 6 kb of 5' flanking sequence reveal most prominent expression and variable tissue pathologies in the testes.

Mice overexpressing the rat mu opiate receptor in catecholamine neurons under the control of 4.8 kb of the rat tyrosine hydroxylase promoter display altered responses to opiate drug administration and withdrawal. These animals display greater morphine analgesic potency and more prominent morphine-induced locomotion when compared to their non-transgenic littermates. They fail to display greatly altered morphine-induced conditioned place preference, but reveal striking differences in the magnitude of naloxone-precipitated withdrawal from chronic morphine treatment.

These transgenic animals enhance understanding of brain systems prominently involved in opiate drug actions.

Source: https://www.industrydocuments.ucsf.edu/docs/sgwb0000